REMARKS

The Office Action of January 30, 2004, has been received and reviewed. Claims 1-2, 6, 9-11, 13-31, 33-37 and 40-43 are pending in the application. Claims 23, 25 and 26 have been withdrawn from consideration as being directed to a non-elected invention, and claims 1, 2, 6, 9-11, 13-22, 24, 27-31, 33-37 and 40-43 stand rejected. Claims 2, 9, 10, 13, 14, 30, 40 and 42 have been amended, claims 1, 6, 11, 33, 34, 36, 37 and 41 have been canceled, and new claims 44-49 have been added as set forth herein. All amendments and cancellations are made without prejudice or disclaimer. Reconsideration is requested.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 1-2, 6, 9-11, 13-22, 24, 27-31, 33-37 and 40-43 stand rejected under 35 U.S.C. § 112, first paragraph, as assertedly lacking enablement for an antibody or fragment thereof which binds to an epitope and is broken from an epitope under broadly recited conditions. Claims 1, 6, 11, 33, 34, 36, 37 and 41 have been canceled rendering the rejections thereof moot. Applicants respectfully traverse the rejections as set forth herein.

Specifically, it was thought "that the specification['s] lack of sufficient guidance and predictability in determining on how to make and use an antibody or fragments thereof that [are] able to bind to and [are] broken from an epitope under any broadly recited conditions, the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue," and that the specification lacks enablement for an antibody or fragment thereof "other than under specifically chosen conditions recited in Table 1." (Office Action, page 3). Although applicants do not agree that any of the claims lack compliance with the enablement requirement, to expedite prosecution, independent claim 1 has been canceled and claims 40 and 42 have been amended as set forth herein.

Claim 40 has been amended to be directed to a selected monoclonal antibody, or fragment thereof, wherein: the selected monoclonal antibody, or fragment thereof, has been selected for its ability to bind to an epitope at a first pH of between about 4-6 or 8-8.5; and the selected monoclonal antibody, or fragment thereof, has also been selected such that the bond of the selected monoclonal antibody, or fragment thereof, to the epitope is broken at a second pH of about 7.

Claim 42 has also been amended into independent form and recites in part a selected monoclonal antibody, or fragment thereof, wherein: the selected monoclonal antibody, or fragment thereof, has been selected for its ability to bind an epitope at a first pH of about 8-8.5; and the selected monoclonal antibody, or fragment thereof, has also been selected such that the bond of the selected monoclonal antibody, or fragment thereof, to the epitope is broken at a second pH of about 4-6.

Each of amended claims 40 and 42 is enabled since the as-filed specification teaches one of ordinary skill in the art how to make and use the selected monoclonal antibodies or fragments thereof of claims 40 and 42 without undue experimentation. As stated by the Federal Circuit "enablement is not precluded by the necessity for some experimentation such as routine screening," so long as the "experimentation is not undue." (*In re Wands*, 858 F.2d 731, 736-37, 8 USPQ2d 1400 (Fed. Cir. 1988)). Further, the Board of Appeals stated "the test [of enablement] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed." (*Ex parte Jackson*, 217 USPQ 804, 807 (Bd. of Pat. Appl. & Int. 1982)).

The as-filed specification instructs one of ordinary skill in the art how to select monoclonal antibodies or fragments thereof that specifically bind to an epitope by using a Fab-phage library and helper phages to generate phage particles, wherein the phage particles are screened for their ability to bind the epitope, and, thus, one of ordinary skill in the art may follow the guidance disclosed in the specification to perform the simple screening. (*See*, Specification as-filed, pages 5-7). The specification also discloses a number of phage particles that were able to bind to the epitope under specific conditions, wherein the phage particles were selected and isolated as being specific for binding to the epitope. (*See*, *Id.* at pages 7-9). Further, the as-filed specification provides multiple working examples of selected monoclonal antibodies that are commensurate in scope with claim 40 or claim 42. (*See*, *Id.* at page 7, Table 1).

Thus, one or ordinary skill in the art would be able to make and use the selected monoclonal antibodies or fragments thereof of claim 40 or 42 without undue experimentation.

Reconsideration and withdrawal of the enablement rejections of claims 2, 9-10, 13-22, 24, 27-31, 35, 40 and 42-43 are requested.

In point 4 of the Office Action, claims 1-2, 6, 9-11, 13-22, 24, 27-31, 33-37 and 40-43 were also rejected as assertedly failing to comply with the enablement requirement since it was thought that the specification "does not reasonable provide enablement for any antibody or fragment thereof which binds to an epitope and broken from an epitope from an epitope under any broadly recited conditions for the same reasons set forth in the previous Office Action, mailed 4/22/03." (Office Action at page 3). Further, it was stated that the applicants did not address this issue in the amendment of 10/22/03.

Applicants respectfully request clarification of this rejection because it appears to be the same rejection as point 3 of the instant Office Action. Further, the claims submitted in the amendment of 10/22/03 were not directed to **any** broadly recited conditions, but rather were directed to specified pHs and salt concentrations. However, this rejection should be withdrawn in view of the elements present in amended claims 40 and 42.

Rejections under 35 U.S.C. § 103

Claims 1-2, 6, 9-11, 13-22, 28, 30-31, 33-36 and 40-42

Claims 1-2, 6, 9-11, 13-22, 28, 30-31, 33-36 and 40-42 stand rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over Beggs et al. in view of Goding. Claims 1, 6, 11, 33, 34, 36, 37 and 41 have been canceled rendering the rejections thereof moot. Applicants respectfully traverse the remaining rejections as hereinafter set forth.

Although applicants do not agree that any of the claims are unpatentable in view of the cited references, to expedite prosecution, independent claim 40 has been amended to be directed to a selected monoclonal antibody, or fragment thereof, wherein: the selected monoclonal antibody, or fragment thereof, has been selected for its ability to bind to an epitope at a first pH of between about 4-6 or 8-8.5; and the selected monoclonal antibody, or fragment thereof, has also been selected such that the bond of the selected monoclonal antibody, or fragment thereof, to the epitope is broken at a second pH of about 7.

A *prima facie* case of obviousness cannot be established with regard to amended claim 40 since Beggs et al. does not alone, or in combination with Goding, teach or suggest each and every

element of claim 40. For instance, claim 40 recites in part that the bond between the selected monoclonal antibody or fragment thereof and the epitope is broken at a pH of about 7. Neither Beggs et al. nor Goding teach or suggest a bond between a selected monoclonal antibody of a fragment thereof and an epitope being broken at a pH of about 7.

Beggs et al. discloses that "the first antibody fragment may be suitable to bind to an antigenic component of dental plaque" and does not teach or suggest breaking a bond between the first antibody and the epitope at a pH of about 7. (Beggs et al., Col. 4, lines 22-24). Rather, Beggs et al. teaches the stability of antigen-antibody binding and, thus, teaches away from breaking the bond between the selected monoclonal antibody or fragment thereof and the epitope at a pH of about 7. (*See, Id.* at Col. 5, lines 60-65). Goding is limited to "the binding of polyclonal antibodies to their antigen is usually stable over a wide range of pH (~4-9)" and gives an example of a monoclonal antibody that "bound its antigen at a pH 7.0." (Goding, pages 44-45). Thus, Goding actually teaches away from a bond between a selected monoclonal antibody or a fragment thereof and an epitope being broken at a pH of about 7 as recited in claim 40. Accordingly, the cited references do not alone, or in combination, teach or suggest each and every element of amended claim 40 as required to establish a *prima facie* case of obviousness.

Claims 2, 9, 10, 13-22, 24, 27-30, 35, 43 and 44 are nonobvious, at the very least, as depending from nonobvious independent claim 40. (*See, In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)).

A *prima facie* case of obviousness also cannot be established with regard to amended claim 42 since the cited references do not alone, or in combination, teach or suggest each and every element of claim 42. Amended claim 42 is directed to a selected monoclonal antibody or fragment thereof that binds to an epitope at a first pH of about 8-8.5 and wherein the bond between the selected monoclonal antibody or the fragment thereof and the epitope is broken at a second pH of about 4-6. Beggs et al. does not alone, or in combination with Goding, teach or suggest a selected monoclonal antibody that binds to an epitope at a first pH of about 8-8.5 and wherein the bond is broken at a second pH of about 4-6.

As previously established herein, Goding establishes that polyclonal antibodies are typically stable in the range of pH between 4 and 9 (*See*, Goding, *supra*) and Beggs et al. does not teach or suggest breaking a bond between an antibody and an epitope at a pH of about 4-6.

As stated in Beggs et al., the binding "of the first antibody fragment to the target site [i.e., the epitope] holds the therapeutic agent on the target site, [in order] for the therapeutic agent to act on the target site." (Beggs et al. at Col. 7, lines 10-12). Beggs et al. further indicates that "reducing pH in this [periodontal pocket] cavity would give conditions less favourable for anaerobic organisms which can invade this pocket" and, thus, teaches away from breaking the bond between the selected monoclonal antibody or fragment thereof and the epitope at a pH of about 4-6 because, in order for the therapeutic agent to be effective, the antibody must continue to bind at the lower pH. (*Id.* at Col. 4, lines 63-65).

Since the cited references do not teach each and every element of amended claim 42, a *prima facie* case of obviousness cannot be established. Claims 45-49 are nonobvious, at the very least, as depending from nonobvious independent claim 42. (*See*, *In re Fine*, *supra*). Reconsideration and withdrawal of the obviousness rejections of claims 2, 9-10, 13-22, 28, 30-31, 35, 40 and 42 are requested.

Claims 1-2, 6, 9-11, 13-21, 24, 27, 28, 30, 31, 33-36 and 40-42

Claims 1-2, 6, 9-11, 13-21, 24, 27, 28, 30, 31, 33-36 and 40-42 stand rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over Cummins et al. in view of Goding. Claims 1, 6, 11, 33, 34, 36, 37 and 41 have been canceled rendering the rejections thereof moot. Applicants respectfully traverse the remaining rejections as set forth herein.

A *prima facie* case of obviousness cannot be established with regard to amended claim 40 since the cited references do not, alone or in combination, teach or suggest that the bond between the selected monoclonal antibody or fragment thereof and the epitope is broken at a pH of about 7 as recited in amended claim 40. The antibodies disclosed in Cummins et al. "are substantive (i.e., withstand the flow of saliva), are not inhibited by soluble salivary components and remain reactive vs. their target in the presence of a developing biofilm." (Cummins et al., page 3, lines 30-31). Thus, the antibodies of Cummins et al. do not release at physiological acceptable conditions, such as around pH 7.

Further, Cummins et al. and Goding, when viewed in combination, do not teach or suggest each and every element of amended claim 40. Goding teaches that "the binding of polyclonal antibodies to their antigen is usually stable over a wide range of pH (~4-9)" and gives

an example of a monoclonal antibody that "bound its antigen at a pH 7.0." (Goding at pages 44-45). Thus, Cummins et al. and Goding do not, alone or in combination, teach or suggest each and every element of amended claim 40 as required to establish obviousness.

Claims 2, 9, 10, 13-22, 24, 27-30, 35, 43 and 44 are nonobvious, at the very least, as depending from nonobvious independent claim 40.

Turning to amended claim 42, it is directed to a selected monoclonal antibody or fragment thereof that binds an epitope at a first pH of about 8-8.5 and wherein the bond between the selected monoclonal antibody or the fragment thereof and the epitope is broken at a second pH of about 4-6. Neither Cummins et al. nor Goding, alone or in combination, teach or suggest each and every element of amended claim 42 as required for obviousness.

In fact, Cummins et al. does not teach or suggest any breaking of the bond between the antibody and the epitope, but rather the antibodies are designed to withstand the flow of saliva, are not inhibited by soluble salivary components and remain active against their target in the presence of a developing biofilm. (*See*, Cummins et al., *supra*). Thus, the antibodies of Cummins et al. are chosen to stably bind to their epitope. Further, the combination of Cummins et al. with Goding actually teaches away from the selected monoclonal antibodies or fragments thereof of claim 42 since Goding states that "the binding of polyclonal antibodies to their antigen is usually stable over a wide range of pH (~4-9)." (Goding at pages 44-45). Since the combined references do not teach or suggest each and every element of amended claim 42, claim 42 cannot be rendered obvious.

Claims 45-49 are nonobvious, at the very least, as depending from nonobvious independent claim 42. Reconsideration and withdrawal of the obviousness rejections of claims 2, 9-10, 13-22, 28, 30-31, 35, 40 and 42 are requested.

Claim 29

Claim 29 stands rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over Beggs et al. in view of Goding as applied to claims 1-2, 6, 9-11, 13-22, 28, 30-31, 33-36 and 40-

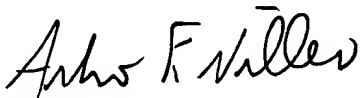
42 as above, and further in view of Cole et al. Applicants respectfully traverse the rejections as set forth herein.

Claim 29 is nonobvious, at the very least, as depending from nonobvious independent claim 40. Reconsideration and withdrawal of the obviousness rejection of claim 29 is, thus, requested.

CONCLUSION

In view of the amendments and remarks presented herein, applicants respectfully submit that the claims define patentable subject matter. Should any questions remain after consideration of the foregoing, the Office is kindly invited to contact the applicants' attorney at the address or telephone number given herein.

Respectfully submitted,



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Date: June 30, 2004
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